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## **Purpuric pityriasis rosea in patients with anorexia nervosa**

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**Contributions:** FD, conceived the presented idea and wrote the first draft of the manuscript; GC, AH, developed the theory and wrote the manuscript; AG, investigated the histological aspects of the exanthem; VA, AH, supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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**Ethics approval and consent to participate:** No ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patients included in this study.

**Consent for publication:** The patient gave their written consent to use their personal data for the publication of this case report and any accompanying images.

**Availability of data and materials:** all data underlying the findings are fully available.

## **Abstract**

Pityriasis rosea (PR) is an exanthematous disease associated with the endogenous systemic reactivation of human herpesvirus (HHV)-6 and/or HHV-7. Variants of PR characterized by atypical lesion morphology, eruption course, and severe symptoms have already been described, but their prevalence is probably underestimated. We report herein two patients suffering from anorexia nervosa (AN) who developed a very rare form of purpuric PR. So far, no cases of PR in AN patients have been reported in the literature.

In AN, impaired cell-mediated immunity may favor the endogenous systemic reactivation of HHV-6 and/or HHV-7, causing PR. Furthermore, an increased level of the vascular cell adhesion molecule 1, interleukin 6, and tumor necrosis factor- $\alpha$  has been demonstrated in AN patients, which may be responsible for their increased vascular dysfunction.

## **Introduction**

Pityriasis rosea (PR) is an exanthematous disease associated with the endogenous systemic reactivation of human herpesvirus (HHV)-6 and/or HHV-7.<sup>1</sup> Forms of PR characterized by atypical lesion morphology, eruption course, and severe symptoms have already been described, but their prevalence is probably underestimated.<sup>1,2</sup> We report herein two patients suffering from anorexia nervosa (AN) who developed a very rare form of purpuric PR. So far, cases of PR in patients with AN have never been described in the literature.

## **Case Reports**

### ***Case 1***

A 17-year-old male presented with a 3-week history of an asymptomatic skin eruption preceded a few days earlier by a sore throat and generalized arthromyalgia. Medical history is remarkable for AN, which started three years earlier. He did not take any medication and was on a program of behavioral psychotherapy for AN. Physical examination showed maculopapular, purpuric lesions of a few millimeters in diameter, sometimes covered with fine scales, coalescing to form annular lesions on the cleavage lines of the trunk (Figures 1 A,B). An erythematous-purpuric scaly plaque (herald patch) on the abdomen had preceded the eruption. Punctate hemorrhages were present on the oral mucous membrane. There was neither lymphadenopathy nor hepatosplenomegaly. Routine blood investigations were normal. The calibrated quantitative real-time polymerase chain reaction (CQ-PCR) detected Epstein-Barr virus DNA (215,000 copy/mL) and HHV-6 (320 genome equivalents/mL) plasma viremia, whereas HHV-7 and cytomegalovirus DNA were not detected in plasma.

## **Case 2**

A 27-year-old female presented with a 2-week history of a severe itchy eruption over the trunk. The eruption was preceded by a few days of headache and difficulty in concentration. She suffered from AN and was being treated with psychotherapy for five years. She was not taking any drugs.

Physical examination showed an erythematous macular and purpuric eruption and widespread scratching lesions over the trunk (Figures 1 C). Routine laboratory investigations were normal, and no virus was found in the plasma by CQ-PCR.

## **Discussion and Conclusions**

Histopathology of a skin biopsy showed foci of spongiosis and a perivascular infiltrate of lymphocytes in both patients, with prominent erythrocyte extravasation in the papillary dermis (Figure 2). A diagnosis of purpuric PR was made in both patients. The eruption was faded in 6 weeks without treatment.

As for other exanthems, in addition to the typical PR presentation, atypical forms have been described.<sup>1,2</sup> Purpuric PR was first reported by Hartman in 1944,<sup>3</sup> and since then, very few cases have been described.<sup>4-6</sup> In purpuric PR, the erythrocyte's extravasation into the papillary dermis is significant and gives rise to the purpuric morphology. The presence of a “curtain theatre” pattern and the absence of histopathological signs of true vasculitis, namely fibrinoid degeneration, neutrophilic infiltrate, and nuclear dust, differentiates this form from pigmented purpuric dermatosis and cutaneous vasculitis.<sup>3</sup>

AN is a psychiatric disorder characterized by malnutrition and is frequently associated with medical complications. Cell-mediated immunity is usually altered in AN, as reflected by lymphocyte subset counts and the response to delayed hypersensitivity tests; leukocyte, lymphocyte, and T-cell counts have been shown to be depleted in AN patients.<sup>4</sup> T-lymphocytes correlate negatively with body mass index and are critically low in patients with severe malnutrition.<sup>7</sup> However, the consequences of these changes remain controversial regarding the susceptibility to infections.<sup>7</sup> In AN, the impaired cell-mediated immunity may favor the endogenous systemic reactivation of HHV-6 and/or HHV-7, causing PR. A decreased ability of the immune system to control other latent infections, such as Epstein-Barr virus (EBV),<sup>8,9</sup> has been hypothesized to be responsible for other AN comorbidities like chronic fatigue syndrome, celiac disease, rheumatoid arthritis, and other autoimmune diseases.<sup>8,10</sup>

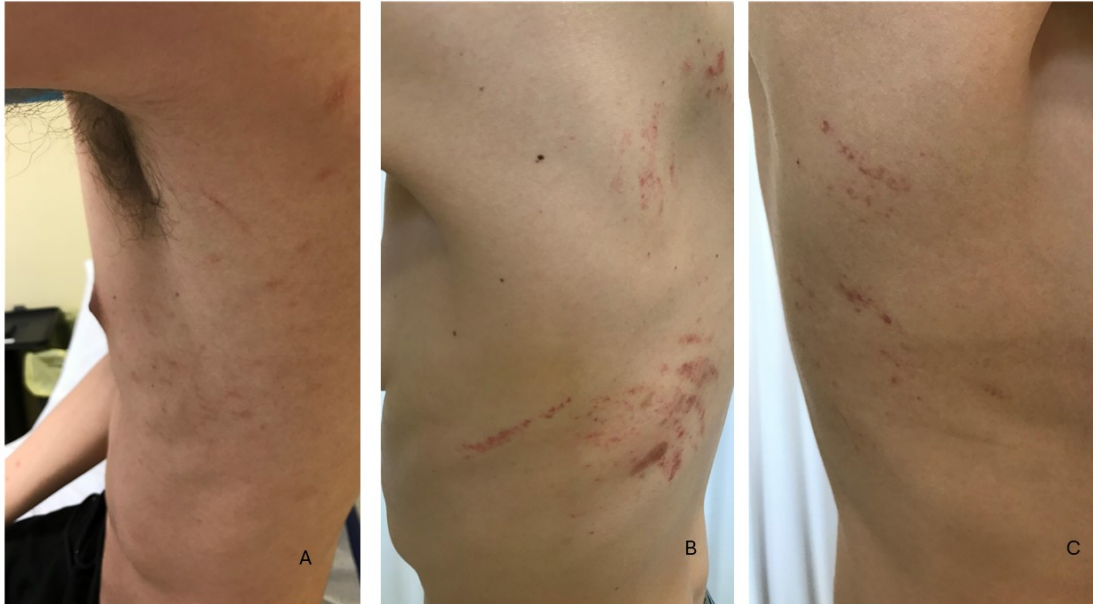
Furthermore, an increased level of the vascular cell adhesion molecule 1, interleukin 6, and tumor necrosis factor- $\alpha$  has been demonstrated in AN patients, which may be responsible for their increased vascular dysfunction.<sup>11</sup> Microvascular damage may, therefore, be the basis for the greater

presence of erythrocyte extravasation into the papillary dermis, which is the histopathological hallmark of the purpuric PR.

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**Figure 1.** A) Purpuric PR in the first reported patient: maculopapular, purpuric lesions of a few millimeters in diameter, sometimes covered with fine scales, coalescing to form annular lesions on the cleavage lines of the trunk (“theatre curtain distribution”); B, C) erythematous macular-purpuric eruption and widespread scratching lesions over the trunk in the second described patient with purpuric PR.



**Figure 2.** Histopathology shows an epidermis with patchy parakeratosis, irregular acanthosis, and mild spongiosis. In the papillary dermis, a perivascular inflammatory infiltrate and extravasated erythrocytes are shown (Hematoxylin and eosin, 20x).

